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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,649	05/23/2001	Julian M.C. Golc	VPI/00-114	1044

27916 7590 11/05/2003

VERTEX PHARMACEUTICALS INC.
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EXAMINER

RUSSEL, JEFFREY E

ART UNIT PAPER NUMBER

1654

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center">Office Action Summary</p>	Application No. 09/863,649	Applicant(s) GOLEC, JULIAN M.C.	
	Examiner Jeffrey E. Russel	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 5-8 and 12-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-3, 5-7, 18-27 and 31-33 is/are allowed.
- 6) ☒ Claim(s) 8, 12-17, 28-30 and 34-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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1. The amendment to the claims filed August 8, 2003 was not in proper format under 37 CFR 1.121(c) because every claim number was not followed by a parenthetical expression indicating the status of the claim. See, e.g., claims 5, 6, 8, 12, and 14-17.
2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either on an application data sheet or supplemental oath or declaration.

The declaration filed November 28, 2001 does not provide a city of residence for inventor Golec.

The request to correct the inventorship of this nonprovisional application under 37 CFR 1.48(a) is deficient because:

The declaration filed September 12, 2003 does not recite a citizenship for Inventor Brenchley.

The statements under 37 CFR 1.48(a) for Inventors Bebbington, Knegt, and Mortimore are missing from the electronic file wrapper. It is possible that the three statements were submitted but not scanned into the electronic file wrapper. In order to expedite prosecution of this application, Applicants are requested to re-submit copies of the statements.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 8, 12-17, 29, 30, and 34-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure supporting the recitation in claims 29 and 30 in the definition of R' that each group can be optionally substituted. Page 11, line 29, - page 12, line 7, of the specification, cited by Applicant as support for the new claim limitations, does not mention such optional substitution.

4. Claims 8, 12-17, and 28 are objected to because of the following informalities: At claim 28, last line, "tetrazolyl" is misspelled. Appropriate correction is required.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 8, 12, 16, 17, 28, and 30 are rejected under 35 U.S.C. 102(e) as being anticipated by Ohmoto et al (U.S. Patent No. 6,136,834). Ohmoto et al teach compounds in Examples 18(23), 18(24), 19(21), and 19(22) which meet the requirements of Applicant's formula I in which R¹ is R which is a substituted aliphatic group or a substituted heterocyclalkyl group. The compounds of Ohmoto et al are ICE inhibitors which are used to treat diseases such as infectious diseases, Alzheimer's disease, AIDS, leukemia, and neoplasm. See, e.g., column 219, line 10 - column 220, line 59; column 414, line 37 - column 415, line 21; column 422, line 42 - column 423, line 26; and claims 13-14. These compounds of Ohmoto et al are also deemed to constitute pharmaceutically acceptable derivatives of the other compounds embraced by Applicant's formula I in view of their structural and functional similarity.

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7. Claims 13-15 are rejected under 35 U.S.C. 103(a) as being obvious over Ohmoto et al (U.S. Patent No. 6,136,834) as applied against claims 8, 12, 16, 17, 28, and 30 above, and further in view of Hagmann et al (U.S. Patent No. 5,866,545) and Baust et al (U.S. Patent No. 6,045,990). Ohmoto et al do not teach using their ICE inhibitors to treat complications associated with coronary artery bypass grafts, or to preserve cells, organs to be transplanted, or blood products. Hagmann et al disclose the use of ICE inhibitors to treat graft rejection and graft-versus-host disease (see, e.g., column 2, lines 38-54). Baust et al disclose the use of caspase protease inhibitors to treat animal or human organs, tissues or cells for hypothermic storage, e.g., prior to transplantation (see, e.g., column 5, lines 58-61; column 16, lines 36-54; and claim 6). It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the ICE inhibitors of Ohmoto et al to treat complications associated with coronary artery bypass grafts, or to preserve cells, organs to be transplanted, or blood products, because Hagmann et al and Baust et al teach that these are known uses for ICE inhibitors; because the ICE inhibitors of Ohmoto et al are structurally and functionally analogous to those described by Hagmann et al and Baust et al; because it is the ability to inhibit ICE, rather than the presence of any particular chemical structure, which would have been expected to be necessary in order to treat graft rejection and graft-versus-host disease as taught by Hagmann et al or to treat animal or human organs, tissues or cells for hypothermic storage as taught by Baust et al; and because it is prima facie obvious to use ICE inhibitors or caspase inhibitors for the same pharmaceutical purposes that other ICE inhibitors and caspase inhibitors are used.
8. Applicant's arguments filed August 8, 2003 have been fully considered but they are not persuasive.

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Claims 28 and 30, and the claims dependent upon them, remain rejected over Ohmoto et al '834 as the primary reference. While claim 28 excludes compounds in which R¹ is -CH₂-tetrazolyl, in the compounds of Ohmoto et al, the corresponding group is a substituted -CH₂-tetrazolyl. An amendment to the proviso clause of claim 28 stating that R¹ is not a substituted -CH₂-tetrazolyl would avoid the rejection of this claim over Ohmoto et al '834. Claim 30 recites that R¹ can be R which can be a substituted heterocyclalkyl group, and this limitation is met by the substituted -CH₂-tetrazolyl group in the compounds of Ohmoto et al '834.

9. Claims 1-3, 5-7, 18-27, and 31-33 are allowed. Claims 29 and 34-42 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, first paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

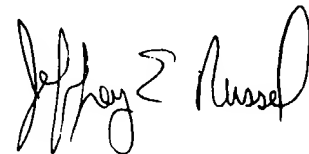
10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

A handwritten signature in black ink, appearing to read "Jeffrey E. Russel". The signature is stylized with a large, looped "J" and a cursive "Russel".

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

November 3, 2003